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Diabetes Study Verifies Lifesaving Tactic

By GINA KOLATA

A 17-year federal study has finally answered one of the most pressing questions about diabetes: Can tight control of blood sugar prevent heart attacks and strokes?

The answer, reported today in The New England Journal of Medicine, is yes. Intense control can reduce the risk by nearly half.

And, the study found, the effect occurred even though the patients had only had a relatively brief period of intense blood sugar control when they were young adults. Nonetheless, more than a decade later, when they reached middle age, when heart disease and strokes normally start to appear, they were protected.

The study involved those with Type 1 diabetes, which usually arises in early in life and involves the death of insulin-secreting cells.

"This is truly an important study," said Dr. Robert Rizza, a professor of medicine at the Mayo Clinic and the president of the American Diabetes Association. "And I usually don't say that," he added.

The findings are likely to affect clinical practice, encouraging doctors to put more effort into helping patients control their blood sugar, said Dr. John B. Buse, the director of the diabetes care center at the University of North Carolina.

The study is "the most rigorously conducted to date," Dr. Buse said, and its authors are "exceptionally well known in the diabetes and medical world."

The question of whether rigid blood sugar control protects against heart disease and strokes has plagued the field for decades, diabetes researchers said.

"It's really a major question that has been around for a long time," said Dr. Judith Fradkin, who directs diabetes research at the National Institute of Diabetes and Digestive and Kidney Diseases.

Researchers knew that diabetes was linked to heart disease - at least two-thirds of diabetics die of heart disease. But although studies showed that controlling blood sugar protected against damage to the eyes, kidneys and nerves, there was no conclusive evidence that it would have the same effect on heart disease and stroke.

"In that sense, this is a landmark study," said Dr. William Cefalu, a diabetes researcher at the Pennington Biomedical Research Center in Baton Rouge, La., who wrote an editorial accompanying the paper.

The study began with 1,441 people aged 13 to 39. Half were randomly assigned to intensive therapy, intended to keep their blood sugar levels low all the time. That meant injecting themselves with insulin three or more times a day or using an insulin pump to infuse the hormone.

The others were assigned to conventional therapy, which meant one or two insulin injections a day, a regimen that was easier for patients but resulted in higher sugar levels.

Blood sugar was assessed by measuring the amount of hemoglobin A1c in the participants' blood, a test that looks for hemoglobin with sugar attached to it. The goal for the intensive-therapy group was to keep those levels to 6 percent or less. They achieved an average level of 7 percent.

Those assigned to conventional treatment had an average level of 9 percent. Normal levels for people without diabetes are 4 percent to 6 percent.

After six and one-half years, both groups were told that intensive therapy had prevented injury to the eyes, kidneys and nerves but that it had not found an effect on heart attacks and strokes.

Those who had had the conventional treatment were taught the intensive treatment regimen. Then, for the next 11 years, all the patients were followed but left to their own doctors' care. Soon the two groups had about the same hemoglobin A1c levels, about 8 percent.

As the years went by and the patients started developing signs of heart disease, the researchers noticed a pronounced difference between the two groups in their rates of heart attack and stroke. Thirty-one of the patients who had had intensive treatment when they were young had a total of 46 cardiovascular events, including heart attacks, stroke and heart disease severe enough to require bypass surgery. Fifty-two of the conventionally treated patients had a total of 98 such events.

"It was amazing," said Dr. David Nathan, a diabetes researcher at the Massachusetts General Hospital who was co-chairman of the study. "Therapy for six and one-half years seems to have driven a dramatic effect."

But the result also gives rise to questions: Does the same effect occur in people with Type 2 diabetes, which usually occurs later in life and involves an inability to respond to insulin? And why would tight control of blood sugar for one brief period have such a pronounced effect later?

Dr. Fradkin said she expected that the results would hold for Type 2 diabetes. Another large federal study is addressing that question, she noted, but it is already known that tight control of blood sugar in Type 2 diabetes protects against nerve, kidney and eye damage, just as it does with Type 1 diabetes.

In addition, a study in Britain hinted, though it did not demonstrate, that Type 2 diabetics who kept their blood sugar low had less heart disease and fewer strokes.

But why controlling blood sugar for a brief period would have such a pronounced effect is a mystery, researchers say. "To me, the observation is fascinating," Dr. Buse said.

The immediate problem, Dr. Fradkin said, is that fewer than 40 percent of diabetics are keeping their hemoglobin A1c levels at 7 percent or below.

Such levels are not easy to obtain, Dr. Cefalu said. "There are side effects - hypoglycemia, weight gain."

"We want patients to say to their doctor, 'What is my A1c level? What should it be? And what can I do to get it there?' " Dr. Fradkin said.